IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of	: Meyer, O. et al	) Art Unit:	1625
Serial No.	: 10/075,956	) Examiner:	Owens, A. A.
Confirmation No.	: 9825		
Filed	: February 14, 2002		
For	: Continuous Process for Preparing Dihydropyrones		
Docket No.	: 1/1190 US		

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO OFFICE ACTION

In response to the Office Action dated 10/24/2005, please reconsider the above-identified application in view of the following:

Remarks/Arguments which begin on page 2 of this paper.

Claims 1-11 are pending.

Claims 1-11 have been rejected under 35 USC 103(a) as being allegedly unpatentable over Turner (J. Med Chem.) and Ehrfeld. This rejection is traversed for all the reasons provided in the previous paper by applicants, and the following.

In the Office Action Applicants it is alleged that Ehrfeld provides the requisite motivation to modify the teachings of Turner by applying micromixers to the reaction.

As applicants pointed out in the last paper, Ehrfeld's et al. article does not teach or suggest that such micromixers are advantageously suitable for preparing dihydropyrones according to the general formula (I). The reaction as described by Turner et al. starts with a slurry which is not suited to be employed in a micromixer as it would plug the narrow channels of the mixing elements. The Examiner has alleged that because a 'slurry' is, as defined by Hawleys Condensed Chemical Dictionary, "a thin watery suspension", that it it would have been perfectly suitable for use in a micromixer. Applicants respectfully disagree. As defined by Hawleys, a slurry is a **suspension**, and not a solution. All slurries are therefore not clear, filtered and suspended in water as are solutions. According to Wikipedia (http://en.wikipedia.org/wiki/Suspension_%28chemistry%29), a suspension is a colloidal dispersion (mixture) in which a finely-divided species is combined with another species, with the former being so finely divided and mixed that it doesn't rapidly settle out. It then adds that the most common suspensions are those of solids in liquid water and that it is important to distinguish suspensions from solutions. In solutions there is no separation over any period of time because the intermolecular forces between the different types of molecules are of similar strength to the attraction between molecules of the same type. Entropy is then sufficient to keep a solution mixed without the need for the external input of energy, which a suspension requires.

To further support applicants contention that one would of ordinary skill in the field would not consider using a slurry in a microreactor, K.-P. Kämper et al. Microfluidic components for biological and chemical microreactors", submitted on the record previously, states on page 340, right column, at the bottom:

"Microfluidic systems, incorporating e.g. .... require the use of very clean and essentially particle-free fluids."

The evidence above, and that provided by the Examiner, does not point to a slurry as being ideal for microreactors.

Further, the disclosure of Ehrfeld on page 1075, second paragraph teaches away from modifying the reaction of Turner et al. (which requires a reaction time of 1 h at 0°C) with applying micromixers/microreactors:

"…It was pointed out by different authors that a great potential of such mixers is mixing in *extremely short time intervals*, that is, in the range of 1 s down to a few milliseconds."(italics added for emphasis).

Ehrfeld describes the mixing quality of a single mixing unit and mixer arrays having various designs. For the characterization a fast inorganic reaction was employed wherein the iodine concentration was detected by UV-vis spectroscopy. In the introductionary part of the article the authors very generally state a great potential of such mixers.

The general advantage of micromixers is to carry out chemical reactions which demand a high heat flow, i.e. which otherwise would be to fast or even uncontrollable. Therefore, in the present case one skilled in the art would not consider the reaction as presented by Turner et al. to be advantageously transferred to micromixers.

As stated above, the reaction time given by Turner is **1h** at 0°C. This is magnitudes longer than what is achieved with the present invention (**0.37 min**). The reaction time can be calculated as follows:

According to the Example 1 of the present invention, the volume flow is 1 ml/min of mixture I and 1.1 ml/min of mixture II, i.e. 2.1 ml/min of the resulting mixture.
The capillary has a length of 1m and a diameter of 1 mm. The reaction solution is passed through this capillary and then taken up in a solution at a pH 5-6. The reaction thus takes place in the capillary.

The volume of the capillary is: (1000 mm*π* (0.5mm)^2)=785(mm)^3 = 0.78ml. The volume of the micro mixer is ca. 15 µl which can be neglected compared with the volume of the capillary.

The reaction time is (assuming that it takes from the start to the end of the capillary to react completely):
0.78/2.1 Min = **0.37 Min.**

As mentioned in the previous paper, the inventors have also surprisingly found that by carrying out the reaction according to the present invention a high yield of the product in a high purity can be obtained. According to the example 1 a yield of **92%** was obtained although the reaction product of the first step was not purified but directly employed in the second step. Even variations of the reaction conditions resulted in high yields between 82 and 88%. Against this background it is surprising that yields were obtained which are considerably higher than **72%** as obtained by Turner et al. However, this comparison was not commented on by the Examiner.

In view of the foregoing withdrawal of the rejection is respectfully requested.

Respectfully submitted,

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